REMARKS

Favorable reconsideration is respectfully requested in view of the following remarks. Claims 23 and 25 have been amended. The amendments to claims 23 and 25 are supported by the original disclosure, for example by page 21, lines 9-16 of the specification. Claims 27-32 have been canceled without prejudice or disclaimer. Claims 23-26 are pending.

Claims 23-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hashimoto et al. (WO 02/44167). Applicants respectfully traverse the rejection.

Claim 23 recites keeping 0.5 or 1.5 hydrated crystals of optically active isomer (R-isomer) of lansoprazole at about 20 to about 100°C for a time sufficient to produce an amorphous optically active isomer of lansoprazole. Applicants have found that an amorphous optically active isomer of lansoprazole can be produced conveniently from 0.5 or 1.5 hydrated crystals of R-isomer of lansoprazole.

The rejection refers to page 8, lines 15-23 and page 14, lines 1-5 and contends that since Hashimoto teaches the claimed elements, it would have been obvious to achieve the features of claim 23. However, none of the processes taught by Hashimoto corresponds to the process of claim 23. The rejection concedes that Hashimoto does not expressly teach the process of claim 23, but appears to take the position that since Hashimoto teaches the claimed components, it would have been obvious to rearrange the claimed components taught by Hashimoto and achieve the features of claim 23 with a reasonable expectation of success. Applicants respectfully submit that the rejection's conclusion is based on speculation, and therefore, the rejection has not established a prima facie case of obviousness. *See, e.g., Ex parte* Sailer et al., Appeal 2008-2041, p.8 (2008) (holding that there was no prima facie case of obviousness where reasoning is based on speculation).

In particular, at page 8, lines 15-23, Hashimoto mentions only once in the entire disclosure and within a parenthetical that an amorphous material can be used. Hashimoto does not provide any details as to how the amorphous of (R)-lansoprazole is obtained, and in fact indicates that the amorphous (R)-lansoprazole is used as a starting material, and not the final product.

At page 14, lines 1-5, Hashimoto teaches that a crystal of (R)-lansoprazole is dried, but Hashimoto clearly indicates that the final product obtained from drying the crystal of (R)-lansoprazole is a crystal with a specific peak (see page 9, line 30 to page 10, line 4 of

Hashimoto), which is exactly the opposite result of what is recited in claim 23. That is, claim 23 recites that keeping 0.5 or 1.5 hydrated crystals of R-isomer of lansoprazole leads to an amorphous optically active isomer of lansoprazole.

The rejection contends that one of ordinary skill in the art would have been motivated to perform the drying of the crystal of (R)-lansoprazole during the process of routine experimentation, because during the process of routine experimentation, one would store the (R)-lansoprazole at room temperature or would dry the (R)-lansoprazole, which would lead to the formation of an amorphous (R)-lansoprazole. The rejection contends that there would have been a reasonable expectation of success in achieving the features of claim 23 based on the evidence provided by Hashimoto.

Firstly, the evidence provided by Hashimoto clearly establishes the exact opposite of what is claimed in claim 23; that is, that drying a hydrate crystal of (R)-lansoprazole leads to a crystal with a specific peak, as opposed to an amorphous form of (R)-lansoprazole. Thus, the rationale set forth by the rejection, that routine experimentation would lead to the features of claim 23 with a reasonable expectation of success, is clearly inconsistent with the evidence provided by Hashimoto.

Moreover, the rejection's rationale takes the teachings of Hashimoto out of context, and does not consider the teachings of the reference as a whole. The predictable result provided by Hashimoto is that when an amorphous (R)-lansoprazole is used as a starting material, a crystal of lansoprazole is produced, and when a crystal of (R)-lansoprazole is used as a starting material, a crystal of (R)-lansoprazole with a specific peak is produced. Thus, when Hashimoto is considered as a whole, the reference does not provide any reasonable basis to conclude that there would have been a reasonable expectation of success in obtaining an amorphous of (R)-lansoprazole as a product when using a crystal of (R)-lansoprazole as a starting material.

In view of the above, it is clear that the evidence provided by Hashimoto cannot be used as a basis for the conclusion that routine experimentation would lead to a predictable result of producing an amorphous (R)-lansoprazole from a hydrate crystal of (R)-lansoprazole. The rejection has not provided any other evidence in support of this conclusion. As such, Applicants submit that the rejection's conclusion of obviousness is based on speculation, and therefore, the rejection has not established a prima facie case of obviousness. Accordingly, claim 23 and its dependent claims are patentable over Hashimoto.

Claims 23-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujishima et al. (WO 00/78745). Applicants respectfully traverse the rejection.

The rejection refers to page 13, line 30 to page 14, line 16 and page 2, line 32 to page 3, line 3 of Fujishima and contends that since Fujishima teaches the claimed elements, it would have been obvious to achieve the features of claim 23. However, none of the processes taught by Fujishima corresponds to the process of claim 23. The rejection appears to concede that that Fujishima does not expressly teach the process of claim 23, but likewise appears to take the position that since Fujishima teaches the claimed components, it would have been obvious to rearrange the claimed components taught by Fujishima and achieve the features of claim 23 with a reasonable expectation of success. Applicants respectfully submit that the rejection's conclusion is based on speculation, and therefore, the rejection has not established a prima facie case of obviousness.

In particular, the following is provided under Reference Example 1 at page 13, line 30 to page 14, line 12 of Fujishima:

> 2- [[[3-methyl-4- (2,2,2-trifluoroethoxy)-2pyridinyl] methyl] sulfinyl]-lH-benzimidazole (lansoprazole) (racemate) (3.98 g) was dissolved in the following mobile phase (330 ml) and acetonitrile (37 ml) and fractionated by HPLC (column: CHIRALCEL OD 20 mm dia. x 250 mm, temperature: 30 C, mobile phase: hexane/2propanol/ethanol = 255/35/10, flow rate: 16 ml/min, detection wavelength: 285 nm, 1 shot: 20-25 mg). Fractions of optical isomers of shorter retention time were combined and concentrated; the individual lots were combined and dissolved in ethanol and filtered through a 0.45 μm filter; after hexane was added, the filtrate was again evaporated to dryness to yield R (+)-lansoprazole (1.6 g, optical purity > 97.6% ee) as an amorphous substance.

The starting material in Reference Example 1 is "2- [[[3-methyl-4- (2,2,2-trifluoroethoxy)-2pyridinyl] methyl] sulfinyl]-lH-benzimidazole (lansoprazole) (racemate)", which is <u>not</u> a hydrate of lansoprazole. Moreover, Fujishima does not disclose or suggest that a hydrated crystal of lansoprazole can be obtained at any time after fractionating the optical isomers and drying the fractions. In fact, Applicants submit that it is not possible technically to hydrate the lansoprazole after the optical resolution by HPLC of the racemate.

At page 2, line 32 to page 3, line 3, Fujishima teaches that the crystal of (R)-lansoprazole can be a hydrate, but Fujishima clearly indicates that the hydrate crystal of (R)-lansoprazole is the final product, as opposed to being used as a starting material.

The rejection contends that it would have been obvious to use the method of evaporating a hydrate of (R)-lansoprazole to dryness, as taught by Fujishima, and perform the drying at a temperature range of about 20 to 100°C during the process of routine experimentation, and produce the instant invention. The rejection further contends that the amorphous (R)-lansoprazole would be produced necessarily from the process of Fujishima.

Firstly, as indicated above, "2- [[[3-methyl-4- (2,2,2-trifluoroethoxy)-2pyridinyl] methyl] sulfinyl]-lH-benzimidazole (lansoprazole) (racemate)" does not correspond to the 0.5 or 1.5 hydrated crystals of R-isomer of lansoprazole as recited in claim 23. Therefore, Fujishima does not disclose or suggest a "method of evaporating a hydrate of (R)-lansoprazole to dryness" as indicated by the rejection.

Moreover, the rejection's rationale takes the teachings of Fujishima out of context, and does not consider the teachings of the reference as a whole. The predictable result provided by Fujishima is that when an amorphous (R)-lansoprazole is used as a starting material, a stable crystal of lansoprazole can be produced. This is the exact opposite of what is recited in claim 23. Fujishima does not provide any guidance or experimental data where 0.5 or 1.5 hydrated crystals of R-isomer of lansoprazole are used as the starting material. Thus, when Fujishima is considered as a whole, the reference does not provide any reasonable basis to conclude that there would have been a reasonable expectation of success in obtaining an amorphous form of (R)-lansoprazole as a product when using 0.5 or 1.5 hydrated crystals of R-isomer of lansoprazole as a starting material.

In view of the above, it is clear that the evidence provided by Fujishima cannot be used as a basis for the conclusion that routine experimentation would lead to a predictable result of producing an amorphous (R)-lansoprazole from a hydrate crystal of (R)-lansoprazole. The rejection has not provided any other evidence in support of this conclusion. As such, Applicants submit that the rejection's conclusion of obviousness is based on speculation, and therefore, the rejection has not established a prima facie case of obviousness. Accordingly, claim 23 and its dependent claims are patentable over Fujishima.

In view of the above, favorable reconsideration in the form of a notice of allowance is requested. Any questions or concerns regarding this communication can be directed to the attorney-of-record, Douglas P. Mueller, Reg. No. 30,300, at (612) 455.3804.

Respectfully submitted,

HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
P.O. Box 2902
Minneapolis, MN 55402-0902
(612) 455-3800

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By: _____
Douglas P. Mueller
Reg. No. 30,300

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